generates all epithelial cell subsets that comprise a fully functional thymus. Canonical (beta-catenin-mediated) Wnt signaling is involved in many developmental processes, including cell survival, proliferation, migration and polarity. It has also been implicated in thymus development, where recent evidence suggests a role in epithelial cell identity. In the current work we have used a conditional knockout of APC to address the role of Wnt signaling during thymus organogenesis in mice. Loss of APC leads to beta-catenin accumulation and target gene activation, thus mimicking pathway activation via ligand binding. We have knocked out APC, and therefore activated the canonical Wnt pathway, in all thymic epithelial cells from E11.5 of embryonic development. This resulted in a dramatic alteration in thymus structure during embryogenesis. Epithelial cells within the mutant thymus ceased proliferation, no longer formed the characteristic 3D network and showed an altered epithelial marker profile. The mutant thymus was also devoid of lymphocytes, failed to form a vascular network and was encased in a dense mesenchymal capsule. These characteristics are consistent with previous evidence that activation of Wnt signaling in TECs leads to their differentiation to an alternative epithelial cell fate, possibly that of keratinocytes, and we are working to explore this further. We are also interested to determine the molecular mechanisms that underlie this altered epithelial cell fate.

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Program/Abstract # 185
Role of enteric neurons and smooth muscle in development of zebrafish intestinal motility
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Enteric neurons and Interstitial Cells of Cajal (ICC) play a major role in coordination of adult intestinal motility. In mammalian and zebrafish embryos, intestinal motility begins before a complete array of enteric neurons differentiate. In addition, contractility is present in mice and zebrafish embryos even when enteric neurons fail to differentiate. Early motility instead appears to depend more on intrinsic smooth muscle contractility. Changes in serotonin (5HT) modulate motility in the intestine with receptors on both neurons and smooth muscle. Previously, we demonstrated the development of 5HT secreting enteroendocrine cells in the posterior intestinal epithelium along with an anterior to posterior distribution of 5HT containing enteric neurons beginning late during 4 dpf with increases at 5 dpf. Presence of enteroendocrine cells increases posterior 5HT concentration six times higher than anterior as measured by differential pulse voltammetry (DPV). As observed by 5HT immunohistochemistry and DPV, we are able to alter concentrations of 5HT pharmacologically within the intestine. In 5 dpf zebrafish embryos, we have begun to determine the affects of pharmacological alteration of 5HT concentration on intestinal motility. We find that lowering 5HT concentrations changes motility in both anterior and posterior regions however, this response appears to have a neural component in the anterior intestine but not in the posterior.

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Program/Abstract # 186
Augmentation of Smad-dependent BMP signaling in cranial neural crests causes craniosynostosis in mice
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Craniosynostosis is a clinical condition of facial deformity caused by a premature fusion of sutures in an infant skull. Here, we show that enhanced BMP signaling through BMP type IA receptor in neural crests causes premature suture fusion in mice. Ectopic cartilage is found in the frontal suture prior to the fusion suggesting that augmented BMP signaling altered a fate of neural crest stem cells towards chondrocytes. Notably, this phenotype is rescued in a heterozygous null background of Bmpr1a. Phosphorylated SMAD1/5/8, which is higher in the mutant mice, is restored to endogenous levels in the rescued mice. In agreement with this, treatment of selective chemical inhibitor of BMP type I receptor results in a rescue of the craniosynostosis phenotype. These findings demonstrate that augmentation of Smad-dependent BMP signaling directly leads to premature fusion of cranial sutures and appropriate levels of BMP signaling are critical to govern the skull development regulating cell fate of neural crests.

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Program/Abstract # 187
HMGA2 is required in the neural crest cells of *Xenopus laevis*
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HMGA proteins are small DNA binding proteins that use conserved "AT-hook" motifs to interact with DNA to modify chromatin architecture and assist in gene expression. Two HMGAs, HMGA1 and HMGA2, have been described in mammals, encoded by separate genes. These genes are highly expressed in proliferating and undifferentiated tissues during embryogenesis, but not in adult tissues, where they are re-activated in tumor progression. In *Xenopus*, only the hmga2 (Xhmga2) gene is described and localized transcripts are first detected at neurula stages, in the presumptive central nervous system (CNS) and eye field, as well as in the neural crest cell (NCC) presumptive territory. At later stages, Xhmga2 mRNA is detected in the CNS, in the otic vesicles, in migrating neural crest cells and their derivatives, in the notochord and in the medio-lateral mesoderm. We are currently addressing the possible role of Xhmga2 in NCCs. We have injected two different morpholinos targeting Xhmga2 transcripts in the anterior neural region and have observed that injected embryos have a severe disruption of the branchial arches, that are missing or greatly altered. Analysis of NCC molecular markers shows severe downregulation or absence of Xtwist, and Xdll4 expression at the tailbud stage. Extensive cell death occurs in the regions normally occupied by NCC injected embryos. Injection of control mismatched or standard morpholinos did not lead to similar alterations. These data suggest that Xhmga2 is required for NCC survival, possibly during the epithelial–mesenchymal transition and or migratory phase of NCC towards the branchial pouches.

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Program/Abstract # 188
FGF-Ras-MAPK signaling drives apical constriction during zebrafish mechanosensory organ formation
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